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EXAMINER	
HOLT, ANDRIAE M	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/620,404	NTAMBI ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *25 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The new Examiner of record is Andriae M. Holt and can be reached at 571-272-9328. The Examiner acknowledges receipt of the Applicant's Response, which was filed on May 25, 2007, in reply to the Official Action dated November 27, 2006.

Status of Claims

Claims 1-13 were pending in the application. Claims 1-4 and 7-11 have been amended. Claims 12-13 are withdrawn from consideration.

Claims 1-11 will be examined on the merits.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional double patenting rejection of claims 1-5 and 7-10 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1

-9 of copending Application No. 10/094,841 has been overcome by the amendment of claim 1 by adding the "steps of administering an agent for reducing stearoyl-CoA desaturase 1.....and measuring insulin sensitivity and observing an increase in insulin sensitivity following a reduction in SCD1 activity.

The provisional double patenting rejection of claims 1, 8 and 9 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 48 of copending Application No. 11/195561 **is maintained**.

Claims 1, 8 and 9 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 48 of copending Application No. 11/195,561. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to a method of increasing insulin sensitivity in a human or non-human subject by inhibiting the enzymatic activity of SCD1 through administering an SCD1 inhibitor. Claim 48 of application '561 is drawn to a method for treating diabetes and insulin resistance in an individual comprising the step of administering to that individual an inhibitor of an SCD1 protein expression or activity. Both applications are drawn to administering an inhibitor of SCD1 activity for the purpose of treating insulin resistance/increasing insulin sensitivity. Therefore the instant claims are obvious over claim 48 of '561.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments filed May 25, 2007 have been fully considered but they are not persuasive. Applicant has amended claim 1 to recite the additional step of

"measuring insulin sensitivity and observing an increase measure in insulin sensitivity following a reduction in SCD1 activity", and traversed that one skilled in the art had no reason to expect that reducing or inhibiting SCD1 activity would increase insulin sensitivity or to observe an increase in insulin sensitivity as noted on page 6, paragraph 1 of applicant's response. However, it is maintained that by treating diabetes and insulin resistance in an individual comprising the step of administering to that individual an inhibitor of an SCD1 protein expression or activity as stated in claim 48 of Application '561, it would be obvious to one skilled in the art that in order to know or ascertain that the agent being administered is capable of treating diabetes and insulin resistance, that a measurement of its effectiveness would be taken, be it through insulin tolerance tests, intravenous glucose tolerance test or other methods used to test insulin sensitivity. Therefore, the instant claims are obvious over claim 48 of Application '561.

This is a provisional obviousness-type double patenting rejection because the conflict claims have not in fact been patented.

The rejection of claims 1 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is maintained**.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a method of increasing insulin sensitivity in a human or non-human subject by reducing SCD1 activity in the subject through administering an antisense oligonucleotide for SCD1 or an SCD1 inhibitor such as an SCD1 antibody or by inhibiting cytochrome b_5, NADH-cytochrome b_5 reductase, or terminal cyanide-sensitive desaturase. The specification discusses in great detail various assays that could be used to identify potential compounds that reduce SCD1 activity, but does not provide guidance as to which compounds should be screened. At best, it simply indicates that one should run tests on a wide spectrum of compounds in the hope that at least one of them will work. The applicant states, "virtually any number of chemical extracts or compounds can be screened using the exemplary methods described". "Examples of such extracts or compounds include.., plant-, fungal-, prokaryotic-, or animal-based extracts, fermentation broths, and synthetic compounds, - as well as modification of existing compounds" (see page 21, paragraph 83). The applicant further states that "the agent(s) contemplated by the present disclosure includes agents of any size or chemical character, either large or small molecules, including proteins, such as antibodies, nucleic acids, either RNA or DNA, and small chemical structures, such as small organic molecules" (see specification page 22, paragraph 85). However, the specification does not direct a person skilled in the art which compounds have the

desired characteristic of reducing SCD1 activity. See University of Rochester v. G.D. Searle & Co., 68 USPQ2d 1424 (W.D.N.Y. 2003). Therefore, the instant claims and the specification contain no information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention.

Response to Arguments

Applicant's arguments filed May 25, 2007 have been fully considered but they are not persuasive. Applicant has traversed that the written description issue of the patent ('850) cited in University of Rochester is distinguishable from the written description rejection of the application in that the applicants disclose the use of SCD1 knockout (SCD -/-) mice, in which effects of a complete absence of SDC1 were actually described, on page 6, paragraph 3. Applicant further traverses that the written description requirement under § 112 only requires a detailed description of that which is new and that applicant described that inhibition of SCD1, by deletion of the gene, resulted in increased insulin sensitivity independent of the mechanism of SCD1-inhibiting activity and that applicant's and that as this link was previously unknown in the art, applicant's are entitled to a broad scope of protection (page 6, paragraph 4). Applicants further traverse on page 7of the Remarks that actual compounds for inhibiting SCD1 activity are described in the application and three ways to reduce SCD1 activity are described. The Examiner notes that the application does give specific examples of all of the arguments traversed above, however, claims 1 and 8-11 recite administering "an agent" for reducing stearoyl-CoA desaturase 1, which is taken to mean a broad range of compounds, not a specific agent or compound. Applicant's

specification states, "virtually any number of chemical extracts or compounds can be screened using the exemplary methods described". "Examples of such extracts or compounds include.., plant-, fungal-, prokaryotic-, or animal-based extracts, fermentation broths, and synthetic compounds, - as well as modification of existing compounds" (see page 21, paragraph 83). Applicant further states that "the agent(s) contemplated by the present disclosure includes agents of any size or chemical character, either large or small molecules, including proteins, such as antibodies, nucleic acids, either RNA or DNA, and small chemical structures, such as small organic molecules" (see specification page 22, paragraph 85). However, the specification does not direct a person skilled in the art to the vast number of compounds as claimed in claims 1 and 8-11 of the instant invention, but rather to a limited number of which compounds have the desired characteristic of reducing SCD1 activity, such as thiazoladinedione compounds, polyunsaturated fatty acids and an antisense oligonucleotide. Therefore, the instant claims and the specification contain limited information by which a person of ordinary skill in the art would understand that the inventors possessed the claimed invention.

The rejection of claims 1 and 7-11 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement **is withdrawn**.

Applicant's arguments, see page 9 of Remarks, filed May 25, 207, with respect to the rejection(s) of claim(s) 1 and 7-11 under 35 U.S.C. 112, first paragraph have been

fully considered and are persuasive. Therefore, the rejection has been withdrawn.

However, upon further consideration, a new ground(s) of rejection is set forth below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the nature of the invention
2) the state of the prior art
3) the relative skill of those in the art
4) the predictability of the art
5) the breadth of the claims
6) the amount of direction or guidance provided
7) the presence or absence of working examples
8) the quantity of experimentation necessary

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

The nature of the invention

The claimed invention relates to a method of increasing insulin sensitivity in a human or non-human subject by administering an agent for reducing SCD1 activity in the subject, measuring insulin sensitivity and observing an increase in insulin sensitivity. Reduced SCD1 activity in the subject is claimed to result from reduced SCD1 protein level by administering a thiazoladinedione compound, a polyunsaturated fatty acid or an antisense oligonucleotide. While being enabled for a thiazoladinedione compound or a polyunsaturated fatty acid or a specific antisense oligonucleotide, applicant is not enabled for the claimed unspecified "agent" of claims 1-3 and 8-11 and the generic "antisense oligonucleotide" of claim 7.

The state of the prior art

SCD1 is well known in the art as a microsomal enzyme that catalyzes the synthesis of monounsaturated fatty acids by introducing the cis double bond in the delta-9 position of palmitoyl-CoA and stearoyl-CoA. These monounsaturated fatty acids are used as substrates for the synthesis of triglycerides, wax esters, cholesteryl esters and membrane phospholipids.

The predictability of the art

Methods of reducing enzymatic activity in vivo are very difficult to predict. Multiple screening methods are employed to determine which compounds from a library of possibilities have the desired reduction of enzymatic activity in vitro. The compounds are then screened for efficacy in vivo, without undesired side effects. Therefore, considerable experimentation is required to determine an agent efficacy toward a defined enzymatic activity in a desired host.

The breadth of the claims

The instant claims are very broad. The claims are drawn to a method of increasing insulin sensitivity by administering an agent of claim 1 and a generic

antisense oligonucleotide of claim 8. The term "agent" for reducing stearoyl-CoA desaturase 1 can encompass a plethora of species. Similarly, the term antisense oligonucleotide is generic and encompasses a number of oligonucleotides of varying lengths and sequence.

The amount of direction or guidance provided

The specification does not provide a person of ordinary skill in the art with sufficient direction or guidance to practice the claimed invention. The specification does describe specific compounds as noted on page 7, paragraph 2, of Applicant's remarks, that inhibit transcription (e.g., thiazoladine compounds, leptin and polyunsaturated fatty acids) and compounds that can inhibit SCD1 enzymatic activity, paragraph 0032 of the specification. However, there is no guidance or direction on the use of the unspecified "agents" as claimed in claims 1-3 and 8-11.

The quantity of experimentation necessary

To practice the claimed invention, a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success. The invention essentially calls for the use of trial and error to attempt to find a compound that will increase insulin sensitivity in a human or non-human subject by reducing SCD1 activity in the subject. As disclosed by the applicant, "virtually any number of chemical extracts or compounds can be screened using the exemplary methods described". "Examples of such extracts or compounds include.., plant-, fungal-, prokaryotic-, or animal-based extracts, fermentation broths, and synthetic compounds, as well as modification of existing compounds" (see page 21, paragraph 83). Applicant further states that "the agent(s) contemplated by the present disclosure includes agents of any size or chemical character, either large or small molecules, including proteins, such as antibodies, nucleic acids, either RNA or: DNA, and small chemical structures, such as small organic molecules" (see specification page 22, paragraph 85). Therefore, undue experimentation on the part of one skilled in the art would be required to determine

which compounds to administer to reduce stearoyl-CoA desaturase 1 activity in the human or non-human subject with an expectation of success.

Therefore, for the aforementioned reasons, Applicant is not enabled for increasing insulin sensitivity through administering an unspecified "agent" or generic antisense oligonucleotide of claims 1-3 and 7-11.

The rejection of claims 1-4 rejected under 35 U.S.C. 112, first paragraph **is maintained**.

Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for BRL49653, pioglitazone, ciglitazone, englitazone, and troglitazone, does not reasonably provide enablement for thiazoladinedione compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Attention is again directed to In re Wands, 8 USPQ2d 1400 (CAFC 1.988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation.

The instant specification fails to provide guidance that would allow the skilled artisan to practice the instant invention without resorting to undue experimentation, as discussed in the subsections set forth herein below.

The nature of the invention

The claimed invention relates to a method of increasing insulin sensitivity in a human or non-human subject by reducing SCD1 activity in the subject. Reduced SCD1 activity in the subject is claimed to result from reduced SCD1 protein level by inhibiting SCD1

gene transcription through administering a thiazoladinedione compound or a polysaturated fatty acid.

The state of the prior art

SCD1 is well known in the art as a microsomal enzyme that catalyzes the synthesis of monounsaturated fatty acids by introducing the cis double bond in the delta-9 position of palmitoyl-CoA and stearoyl-CoA. These monounsaturated fatty acids are used as substrates for the synthesis of triglycerides, wax esters, cholesteryl esters and membrane phospholipids.

The breadth of the claims

The instant claims are very broad. The claims are directed to a method of administering a thiazoladinedione compound or a polysaturated fatty acid. A thiazoladinedione compound is any compound that has a thiazolidin-2, 4-dione ring structure as part of the molecule, and therefore encompasses a vast number of possible species. Likewise, a polysaturated fatty acid is any compound that contains a polysaturated lipid-carboxylic acid chain, and therefore also encompasses a vast number of possible species.

The amount of direction or guidance provided

The applicant does not provide any direction or guidance with respect to determining which species are defined by the terms thiazoladinedione compound and polysaturated fatty acid. The specification does list some thiazoladinedione compounds, such as BRL49653, pioglitazone, ciglitazone, englitazone, and troglitazone. However, the instant claims are in no way limited to these examples. Unfortunately, the specification does not provide any examples of polysaturated fatty acids, nor any guidance to determine which species are incorporated in its definition.

The quantity of experimentation necessary

To practice the claimed invention, a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success. The instant claims are drawn to numerous species, of which determining the efficacy would require extensive experimental experimentation.

Therefore, for the aforementioned reasons, the applicant, while being enable for BRL49653, pioglitazone, ciglitazone, englitazone, and troglitazone, does not reasonably provide enablement for administering an agent selected from a thiazoladinedione compound and a polysaturated fatty acid.

Response to Arguments

Applicant's arguments filed May 25, 2007 have been fully considered but they are not persuasive. Applicant has traversed that the entire class of thiazoladinedione compounds that are available to one skilled in the art were disclosed and that as a class one skilled in the art understands that thiazoladinediones are organic compounds with a thiazolidine ring and that the Examiner failed to show any example of another thiazoladinedione other than those recited in the application. As applicant notes a thiazoladinedione compound is any compound that has a thiazolidin-2,4-dione ring structure as part of the molecule. The examiner reiterates that thiazolidinedione compounds encompass a vast number of species of compounds. The specification only shows examples of specific thiazoladinediones as these are the only compounds that are enabled by the instant application (see paragraph 0028, Specification) to be administered for reducing stearoyl-CoA desaturase 1 activity. To practice the claimed invention, a person of ordinary skill in the art would have to engage in undue experimentation as the instant claims are drawn to numerous species, of which determining the efficacy would require extensive experimentation, with no assurance of success. Likewise, polyunsaturated fatty acids encompass a vast number of species. The instant application while being enabled for the polyunsaturated fatty acids, cited in the instant invention, i.e. linoleic acid, dodecahexaenoic acid and arachidonic acid (see paragraph 0028, Specification), is not enabled for the entire class of polyunsaturated fatty acids. To practice the claimed invention, a person of ordinary skill in the art would

have to engage in undue experimentation, with no assurance of success. The instant claims are drawn to numerous species, of which determining the efficacy would require extensive experimentation. Therefore, for the aforementioned reasons, applicant, while being enabled for linoleic acid, dodecahexaenoic acid and arachidonic acid, does not reasonably provide enablement for administering an agent selected from general polyunsaturated fatty acids.

The rejection of claim 11 rejected under 35 U.S.C. 112, first paragraph **is withdrawn**.

Applicant's arguments, see page 10, paragraph 3, filed May 25, 2007, with respect to written description under 35 U.S.C. 112, first paragraph have been fully considered and are persuasive. The rejection of claim 11 has been withdrawn per amendment of the claim.

The rejection of claim 4 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is withdrawn**.

Applicant's arguments, see page 10, paragraph 3, filed May 25, 2007, with respect to written description under 35 U.S.C. 112, first paragraph have been fully considered and are persuasive. The rejection of claim 11 has been withdrawn per amendment of the claim, the correction of the typographical error of polyunsaturated fatty acid.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn**.

Applicant's arguments, see page 11, paragraph 1, under Rejections Under 35 U.S.C. § 112, second paragraph, filed May 25, 2007, with respect to indefiniteness under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claims 1-11 has been withdrawn per amendment of the claim, the deletion of the word "sufficiently" from claim 1.

The rejection of claims 1-3, 8 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to lack of an active ingredient or an active step **is withdrawn**.

Applicant's arguments, see page 11, paragraph 2, under Rejections Under 35 U.S.C. § 112, second paragraph, filed May 25, 2007, with respect to claims being incomplete under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claims 1-3, 8 and 11 has been withdrawn per amendment of the claim, the addition of the phrases "administering an agent" in claim 1 and "the agent" in claims 2-4, 8 and 11.

The rejection of claim 6 under 35 U.S.C. 112, second paragraph for insufficient antecedent basis **is withdrawn**.

Applicant's arguments, see page 11, paragraph 3, under Rejections Under 35 U.S.C. § 112, second paragraph, filed May 25, 2007, with respect to claim lacking sufficient antecedent basis under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claim 6 has been withdrawn per amendment of the claim, correction of the typographical error of "polyunsaturated".

The rejection of claim 7 under 35 U.S.C. 112, second paragraph for insufficient antecedent basis **is withdrawn**.

Applicant's arguments, see page 11, paragraph 4 under Rejections Under 35 U.S.C. § 112, second paragraph, filed May 25, 2007, with respect to claims lacking sufficient antecedent basis under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claim 7 has been withdrawn per amendment of the claim, deletion of the phrase "SCD1 protein level is reduced" and to depend on claim 3. The examiner notes that the actual amended claim 7 states method of claim "2". The examiner requests clarification of proper dependent claim, 2 or 3.

The rejection of claim 11 under 35 U.S.C. 112, second paragraph for insufficient antecedent basis **is withdrawn**.

Applicant's arguments, see page 12, paragraph 1, under Rejections Under 35 U.S.C. § 112, second paragraph, filed May 25, 2007, with respect to claim lacking sufficient antecedent basis under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claim 11 has been withdrawn per amendment of the claim, claim recites "the agent" instead of "the inhibitor".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1-5 and 11 rejected under 35 U.S.C. 102(b) as being anticipated by Lehmann et al. (J. Biol. Chem., 1995) **is withdrawn**.

Applicant's arguments, see page 12, Rejections Under 35 U.S.C. § 102, paragraph 1, filed May 25, 2007, with respect to the rejection(s) of claim(s) 1-5 and 11 under 35 U.S.C. § 102 (b) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of amendment of claim by applicant.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Cantello et al. (Journal of Medicinal Chemistry).

The instant claims are drawn to a method of increasing insulin activity in a human or non-human by administering a thiazoladinedione compound selected from the group consisting of BRL49653, pioglitazone, ciglitazone, englitazone and troglitazone. Cantello et al. disclose a series of [(ureidoethoxy)benzyl]2,4-tiazolidinediones and [[heterocyclylamino) alkoxy]benzyl]2,4-thiazolidinediones that were synthesized (Abstract). Cantello et al. disclose antihyperglycemic activity was determined in genetically obese C5 B1/6 ob/ob mice that are insulin resistant, hyperinsulinemic and glucose tolerant. Cantello et al. further disclose compounds were administered in the diet for 8 days and antihyperglycemic efficacy was assessed using an oral glucose tolerance test (page 3979, col. 1). Cantello et al. disclose compounds tested include ciglitazone, pioglitazone, troglitazone and BRL 49653, compound 37 (page 3980, tables

1 and 2). Cantello et al. disclose on page 3981 under Biological Procedures, Determination of Antihyperglycemic Activity, that after 8 days of compound administration, mice were fasted for 5 hrs. A blood sample was taken for glucose analysis. Cantello et al. further disclose glucose was administered by oral gavage. Additional blood samples were added to 1 mL of hemolysis reagent. The glucose concentration in the hemolyzed sample was determined spectrophotometrically with hexokinase/glucose-6-phosphate dehydrogenase using a Ciba-Corning 550 express clinical chemistry analyzer. Cantello et al. further disclose that antihyperglycemic activity is defined as the percentage of reduction in the area under the blood glucose versus time curve (AUC) relative to control animals(page 3981, col. 2). The biological procedures for determining antihyperglycemic activity is a measure of insulin sensitivity, under dynamic conditions, intravenous glucose-tolerance test with minimal model analysis and constant infusion of glucose with model assessment. Therefore, for the foregoing reasons, Cantello et al. anticipate all the limitations of the instant claims.

The rejection of claims 1-4, 6 and 11 rejected under 35 U.S.C. 102(b) as being anticipated by Ntambi et al. (Biochemical and Biophysical Research Communications, 1996) **is maintained**.

Claims 1-4, 6 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Ntambi et al. (Biochemical and Biophysical Research Communications, 1996).

The instant claims are drawn to a method of increasing insulin activity in a human or non-human by administering a polyunsaturated fatty acid selected from the group consisting of dodecahexaenoic acid and arachidonic acid. Ntambi et al. teach the

insulin-stimulated expression of SCD1 mRNA was significantly blunted when the induction medium was supplemented with linolenic acid and arachidonic acid (abstract). Ntambi et al. further teach supplementing with linolenic acid and arachidonic acid repressed induction of SCD1 mRNA by 85% and >90% respectively (page 992, lines 10-11 of the first full paragraph). Ntambi et al. have shown that polyunsaturated fatty acids, including arachidonic acid, inhibit SCD1 gene transcription (page 991, lines 9-11). Because Ntambi et al. have shown arachidonic acid inhibits SCD1 gene transcription; arachidonic acid inherently increases insulin sensitivity. Through inhibiting the transcription of the SCD1 gene with linolenic acid or arachidonic acid, Ntambi et al. are inherently inhibiting the protein cytochrome b_5, NADH-cytochrome b_5 reductase, or terminal cyanide-sensitive desaturase. Therefore, for the foregoing reasons, Ntambi et al. anticipate all the limitations of the instant claims.

Response to Arguments

Applicant's arguments filed May 25, 2007 have been fully considered but they are not persuasive. Applicant has amended claim 1 to recite the step of "measuring insulin sensitivity and observing an increase in insulin sensitivity following a reduction in SCD1 activity". Applicant traverses that prior to applicants' disclosure, one skilled in the art had no reason to expect that reducing or inhibiting SC 1 activity would result in an increase in insulin sensitivity and then to observe an increase. The examiner maintains the rejection as Ntambi et al. disclose on page 992, paragraph 2, that to determine whether the induction by insulin and the inhibitory effect of the PUFAs on SCD1 gene expression was transcriptional, cultured H2.35 cells were transfected with SCD1.CAT4.3. Cells were transfected with RSV.CAT as a control. Ntambi et al. disclose that CAT activity from the SCD1.CAT4.3 fusion gene was low in Williams Medium E containing 5.5mM or 27mM glucose. However, addition of insulin to the culture medium for 36 hrs induced a

2- and 7-fold increase, respectively in CAT activity. Ntambi et al. further disclose that the effects of oleic acid and arachidonic acid on insulin stimulated CAT expression were examined. Ntambi et al. disclose on page 944, paragraph 1, that when compared to albumin control, cells treated with 300 μM arachidonic acid showed a striking 65% decrease in CAT activity. Ntambi et al. further disclose the specificity of insulin and PUFAs was examined by transfecting H2.35 cells with RSV.CAT. The lack of any significant effect on RSV.CAT-transfected cells indicates that the effect of insulin and PUFAs on SCD1 gene transcription is specific for SCD1 gene transcription. Ntambi et al. in this study administered polyunsaturated fatty acid, arachidonic acid, and measured its insulin sensitivity as evidenced by the procedure in paragraph 1, on page 944. Therefore, for the foregoing reasons, Ntambi et al. anticipate all the limitations of the instant claims.

The rejection of claims 1, 7 and 11 rejected under 35 U.S.C. 102(e) as being anticipated by Crooke et al. (US 7,132,529) **is withdrawn**.

Applicant's arguments, see page 12, Rejections Under 35 U.S.C. § 102, paragraph 1, filed May 25, 2007, with respect to the rejection(s) of claim(s) 1, 7 and 11 under 35 U.S.C. § 102 (b) have been fully considered and are persuasive. Therefore, the rejection has been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of amendment of claim by applicant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crooke et al. (US 7,132,529) in view of Monia et al. (US 6,284,538).

Applicant's Invention

Applicant claims a method of increasing insulin sensitivity by administering an agent for reducing stearoyl-CoA desaturase 1 activity to increase insulin sensitivity and then measuring insulin sensitivity and observing an increase in insulin sensitivity following a reduction in SCD1 activity. Applicant further claims the agent is an antisense oligonucleotide for SCD1.

Determination of the scope of the content of the prior art
(MPEP 2141.01)

The teachings of Crooke et al. are incorporated herein by reference and are therefore applied in the instant rejection as discussed hereinabove.

Ascertainment of the difference between the prior art and the claims
(MPEP 2141.02)

Crooke et al. do not teach the measuring of insulin sensitivity. It is for this reason Monia et al. is joined.

Monia et al. teach antisense oligonucleotides, which are targeted to a nucleic acid encoding PTEN, and which modulate the expression of PTEN (col. 3, lines 29-31). Monia et al. teach in example 25, col. 50, lines 7-29, the effects of antisense inhibition of PTEN (ISIS 116847) on Blood Glucose Levels of db/db Mice-insulin Tolerance Test. Monia et al. further teach the process by which the mice were treated

and insulin tolerance tested (lines 10-19). Monia et al. teach that these studies indicate that the PTEN antisense oligonucleotide is capable of increasing sensitivity to insulin (decreasing insulin resistance) and that treatment does not cause hypoglycemia. Monia et al. further teach in claim 27 a method of increasing insulin sensitivity in a diabetic animal comprising administering to said diabetic animal an antisense oligonucleotide.....wherein the expression of PTEN is inhibited and insulin sensitivity is increased (col. 72, lines 58-62).

Finding a prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time the invention to combine the teachings of the two cited references to provide a method of administering an antisense oligonucleotide to reduce stearoyl-CoA desaturase 1 activity to increase insulin sensitivity and measure the insulin sensitivity and observe an increase in insulin sensitivity because Crooke et al. teach antisense oligonucleotide compounds that are capable of inhibiting the expression of human SCD comprising contacting the cells or tissues with an antisense oligonucleotide and that SCD has been implicated in various diseases including diabetes and Monia et al. teach a method of administering an antisense oligonucleotide to increase insulin sensitivity in diabetic mice and a method of measuring insulin sensitivity after administering the antisense oligonucleotide. One would have been motivated to make this combination in order to receive the expected benefit of administering an antisense oligonucleotide that is capable of reducing SCD1 activity, thereby increasing the insulin sensitivity, decreasing

the insulin resistance and being able to effectively measure that increase. Given the state of the art as evidenced by the teaching of the cited references, and absent any evidence to the contrary, there would have been a reasonable expectation of success in combining the teachings of the cited references to produce an effective oligonucleotide antisense that is specific to reducing stearoyl-CoA desaturase 1 to decrease insulin resistance in a diabetic patient, that will improve their ability to more effectively control their glucose levels by increasing the amount of insulin circulating in the system and inevitably, improving the quality of life of the patient by decreasing the likelihood of hyperglycemic incidences and the other health related illness related to diabetes.

The rejection of claims 1-5, 7-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Ntambi et al. (US 2003/0064950 A-1) **is withdrawn**.

Applicant's arguments, see page 12, Rejections Under 35 U.S.C. § 102, paragraph 1, filed May 25, 2007, with respect to the rejection(s) of claim(s) 1-5 and 7-11 under 35 U.S.C. § 102 (b) have been fully considered and are persuasive per applicant's amendment of claim 1 to add the step of administering an agent and measuring insulin sensitivity.

The rejection of claims 1 and 8-11 under 35 U.S.C. 102(e) as being anticipated by Hayden et al. (US 2003/0157552 A1) **is maintained**.

Claims 1 and 8-11 rejected under 35 U.S.C. 102(e) as being anticipated by Hayden et al. (US 2003/0157552 A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The instant claims are drawn to a method of increasing insulin sensitivity through administering an SCD1 antibody. Hayden et al. disclose a method of treating diabetes or insulin resistance through administering an inhibitor of an SCD1 protein expression or activity (claim 48). Through treating insulin resistance, Hayden et al. are increasing insulin sensitivity. Also, through inhibiting SCD1 protein activity, Hayden et al. are inherently inhibiting one of the proteins cytochrome b_5, NADH-cytochrome b_5 reductase, or terminal cyanide-sensitive desaturase. Therefore, for the foregoing reasons, Hayden et al. anticipate all the limitations of the instant claims.

Response to Arguments

Applicant's arguments filed May 25, 2007 have been fully considered but they are not persuasive. Applicant has traversed and has amended claim 1 to recite the additional step of "measuring insulin sensitivity and observing an increase measure in insulin sensitivity following a reduction in SCD1 activity", and traversed that one skilled in the art had no reason to expect that reducing or inhibiting SCD1 activity would increase insulin sensitivity or to observe an increase in insulin sensitivity as noted on page 12, paragraph 4 of applicant's response. However, it is maintained that by treating diabetes and insulin resistance in an individual comprising the step of administering to that individual an inhibitor of an SCD1 protein expression or activity as stated in claim 48 of Hayden et al., it would be obvious to one skilled in the art that in order to know or

ascertain that the agent being administered is capable of treating diabetes and insulin resistance, that a measurement of its effectiveness would be taken, be it through insulin tolerance tests, intravenous glucose tolerance test or other methods used to test insulin sensitivity.

None of the claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is 571-272-9328. The examiner can normally be reached on 7:00 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Richter Johann can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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